

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Sanford M. Simon		POSITION TITLE Professor, Head of Laboratory	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Princeton University	BA	1977	Neuroscience
NYU Medical Center	MA	1980	Physiology & Biophysics
NYU Medical Center	Ph. D.	1984	Physiology & Biophysics
Rockefeller University	Postdoc	1984-1989	Cell Biology/Gunter Blobel

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

2001 – present. Professor, The Rockefeller University.

1994 – 2000. Associate Professor, The Rockefeller University Walter Annenberg Research Professor

1989 – 1994. Assistant Professor, The Rockefeller University

1984 – 1989. Post-doctoral associate, The Rockefeller University with Gunter Blobel.

1977 – 1984. Graduate Student, Dept of Physiology & Biophysics, NYU Medical Center with Rodolfo Llinas.

1972 – 1977. Undergraduate, Princeton University Research with Alan Gelperin & Barry Jacobs.

Numerous awards – most recently the Bard Medal of Science, 2004.

B. Selected peer-reviewed publications (in chronological order). Do not include publications submitted or in preparation (abbreviated list).

J. Z. Rappoport, A. Benmerah and S. M. Simon. Analysis of the AP-2 adaptor complex and cargo during clathrin-mediated endocytosis (2005) Traffic, in press.

H. Tetsuo Uyeda, Igor L. Medintz, Jyoti, K. Jaiswal, Sanford M. Simon and Hedi Mattoussi. Synthesis of Compact Multidentate Ligands to Prepare Stable Hydrophilic Quantum Dot Fluorophores. (2005). J Am Chem Soc (in press)

E. B. Voura, J. K. Jaiswal, H. Mattoussi, and S. M. Simon. Tracking metastatic tumor cell extravasation with quantum dot nanocrystals and fluorescence emission-scanning microscopy. Nat.Med. 10 (9):993-998, 2004.

Jaiswal, J.K. et al (2004) The use of quantum dots for live cell imaging. Nature Methods (in press, Oct 2004)

J. K. Jaiswal and S. M. Simon. Potentials and pitfalls of fluorescent quantum dots for biological imaging. Trends Cell Biol. 14 (9):497-504, 2004.

J. K. Jaiswal and S. M. Simon. (2004). Imaging with quantum dots. In Imaging in Neuroscience (Yuste, R. and Konnerth, A., Eds), Cold Spring Harbor Laboratory Press chapter 77.

J. K. Jaiswal, S. Chakrabarti, N. W. Andrews, and S. M. Simon (2004). Synaptotagmin VII Restricts Fusion Pore Expansion during Lysosomal Exocytosis. PLoS.Biol. 2 (8):E233- (published on line, not yet in print)

M. Fix, T. J. Melia, J. K. Jaiswal, J. Z. Rappoport, D. You, T. H. Sollner, J. E. Rothman, and S. M. Simon (2004). Imaging single membrane fusion events mediated by SNARE proteins. Proc.Natl.Acad.Sci.U.S.A 101 (19):7311-7316.

J. Z. Rappoport, S. M. Simon, and A. Benmerah. Understanding Living Clathrin-Coated Pits (2004). Traffic 5 (5):327-337.

M. S. Wollenberg and S. M. Simon. Signal sequence cleavage of peptidyl-tRNA prior to release from the ribosome and translocon. J.Biol.Chem. 279 (24):24919-24922, 2004.

H. Mattoussi, I. L. Medintz, A. R. Clapp, E. R. Goldman, J. K. Jaiswal, S. M. Simon, and J. M. Mauro (2004). Luminescent Quantum Dot-Bioconjugates in Immunoassays, FRET, Biosensing and Imaging Applications. Journal of the Association for Laboratory Automation 9:28-32.

J. K. Jaiswal, H. Mattoussi, J. M. Mauro, and S. M. Simon (2003). Long-term multiple color imaging of live cells using quantum dot bioconjugates. Nat.Biotechnol. 21 (1):47-51.

J. Z. Rappoport and S. M. Simon. (2003) Real-time analysis of clathrin mediated endocytosis during cell migration. J.Cell Sci. 116:847-855.

J. Z. Rappoport, B. W. Taha, and S. M. Simon. Movement of Plasma-Membrane-Associated Clathrin Spots Along the Microtubule Cytoskeleton. Traffic. 4 (7):460-467, 2003..

J. Z. Rappoport, B. W. Taha, S. Lemeer, A. Benmerah, and S. M. Simon. The AP-2 complex is excluded from the dynamic population of plasma membrane-associated clathrin. J.Biol.Chem. 278 (48):47357-47360, 2003.

G. Kreitzer, J. Schmoranzer, SH Low, X Li, Y Gan, T Weimbs, SM Simon, and E. Rodriguez-Boulan. Three-dimensional analysis of post-Golgi carrier exocytosis in epithelial cells. *Nat.Cell Biol.* 5 (2):126-136, 2003.

J. Schmoranzer and S. M. Simon (2003) . Role of microtubules in fusion of post-Golgi vesicles to the plasma membrane. *Mol.Biol.Cell* 14 (4):1558-1569. December 25, 2002, 10.1091/mbc.E02-08-0500.

J. Schmoranzer, G. Kreitzer, and S. M. Simon. Migrating fibroblasts perform polarized, microtubule-dependent exocytosis towards the leading edge. *J.Cell Sci.* 116 (Pt 22):4513-4519, 2003.

E. M. Kanner, M. Friedlander, and S. M. Simon (2003). Co-translational Targeting and Translocation of the Amino Terminus of Opsin across the Endoplasmic Membrane Requires GTP but Not ATP. *J.Biol.Chem.* 278 (10):7920-7926, 2003.

A. Rajagopal and S. M. Simon. Subcellular localization and activity of multidrug resistance proteins. *Mol.Biol.Cell* 14 (8):3389-3399, 2003.

J. K. Jaiswal, N. W. Andrews, and S. M. Simon. (2002) Membrane proximal lysosomes are the major vesicles responsible for calcium-dependent exocytosis in nonsecretory cells. *J.Cell Biol.* 159 (4):625-635.

E. M. Kanner, I. K. Klein, M. Friedlander, and S. M. Simon (2002). The amino terminus of opsin translocates "Posttranslationally" as efficiently as cotranslationally. *Biochemistry* 41 (24):7707-7715.

N. F. De Souza and S. M. Simon (2002) . Glycosylation Affects the Rate of Traffic of the Shaker Potassium Channel through the Secretory Pathway. *Biochemistry* 41 (38):11351-11361.

A. Rajagopal, A. C. Pant, S. M. Simon, and Y. Chen. (2002) In Vivo Analysis of Human Multidrug Resistance Protein 1 (MRP1) Activity Using Transient Expression of Fluorescently Tagged MRP1. *Cancer Res.* 62 (2):391-396.

Y. Chen, A. C. Pant, and S. M. Simon. (2001) P-glycoprotein does not reduce substrate concentration from the extracellular leaflet of the plasma membrane in living cells. *Cancer Res.* 61 (21):7763-7769.

M. A. Lampson, J. Schmoranzer, A. Zeigerer, S. M. Simon, and T. E. McGraw (2001) . Insulin-regulated Release from the Endosomal Recycling Compartment Is Regulated by Budding of Specialized Vesicles. *Mol.Biol.Cell* 12 (11):3489-3501.

D. K. Marciano, M. Russel, and S. M. Simon (2001) . Assembling filamentous phage occlude pIV channels. *Proc.Natl.Acad.Sci.U.S.A.* 98 (16):9359-9364.

Goulian, M. and S. M. Simon (2000). Tracking single proteins within cells. *Biophys.J.* 79:2188-2198.

Chen, Y. and Simon, S.M. (2000). "In situ biochemical demonstration that P-glycoprotein is a drug efflux pump with broad specificity." *The Journal of Cell Biology* 148:863-870.

Schmoranzer, J., Goulian, M., Axelrod, D., Simon, S.M. (2000). "Imaging constitutive exocytosis with total internal reflection fluorescence microscopy". *The Journal of Cell Biology* 149:23-31.

Kahl, B.C., M. Goulian, W. van Wamel, M. Herrmann, S. M. Simon, G. Kaplan, G. Peters, and A. L. Cheung (2000). *S. aureus* RN6390 replicates and induces apoptosis in a pulmonary epithelial cell line. *Infect.Immun.* 68 (9):5385-5392.

Simon, S.M. (1999). "An award for cell biology". *The Journal of Cell Biology* 147(5) Nov. 29th, 1999.

Chen, Y., Schindler, M. and Simon, S.M. (1999) "A mechanism of tamoxifen inhibition of acidification" *Journal of Biological Chemistry* 274 18364-18373.

Marciano,D, Russel,M, Simon,SM(1999) "An aqueous channel for export of filamentous phage". *Science* 284:1516-19.

Altan,N. Chen,Y., Schindler,M. and Simon,S.M.. (1999) "Tamoxifen Inhibits Acidification in Cells Independent of the Estrogen Receptor" *Proc. Natl. Acad. Sci. USA* 96:4432-4437.

Altan,N., Chen,Y., Schindler,M. and Simon.S.M.. (1998) Defective acidification in human breast tumor cells and implications for chemotherapy. *Journal of Experimental Medicine*, 187:1583-1598.

Simon, S.M. (1996) Cellular Probes on the Move. *Nature Biotechnology* 14 (10) 1221.

Borel, A.C. and Simon, S.M. (1996). Biogenesis of polytopic membrane proteins: Transmembrane segments of P-glycoprotein translocate sequentially across the ER. *Cell* 85, 379-389.

Borel, A.C. and Simon, S.M. (1996). Biogenesis of Polytopic Membrane Proteins: Membrane segments of P-glycoprotein sequentially translocate to span the ER membrane. *Biochemistry* 35 (33) 10587-10594.

Simon, S.M. (1996). Protein-conducting channels for the translocation of proteins into and across membranes. *Cold Spring Harbor Symposia on Quantitative Biology* 60, 57-69.

Schindler, M., Grabski, S., Hoff, E., and Simon, S.M. (1996). Defective pH regulation of acidic compartments in human breast cancer cells (MCF-7) is normalized in adriamycin resistant cells (MCF-7adr). *Biochemistry* 35, 2811-2817.

Simon, S.M. 1994. Ion Channels. Enter the 'swinging gate'. *Nature* 371:103-104.

Simon, S.M., M. Schindler 1994. The cell biology of multidrug resistance in tumors. *PNAS* 91:3496-3504.

Simon, S.M., D. Roy, M. Schindler. 1994. pH and the control of multidrug resistance. *PNAS* 91:1128-1132.

Simon, S. M. 1993. Translocation of proteins across the endoplasmic reticulum *Curr Opin Cell Biol* 5:581-8.

Simon, SM, and G. Blobel. 1992 Signal peptides open protein-conducting channels in E.coli. *Cell* 69:677-84

Simon, S.M., Peskin, C., Oster, G.F. 1992. What drives the translocation of proteins. *PNAS* 89:3770-3774.

Simon, S.M., and Aderem,A. 1992. Myristoylation of proteins in yeast secretory mutants. *J B C* 267:3922-3931.

Lew, D.J.; Simon, S.M. 1991. Characterization of constitutive exocytosis in yeast. *J Memb Biol* 123:261-268.

Simon, SM, and G. Blobel 1991. A protein conducting channel in the endoplasmic reticulum. *Cell* 65:371-380.

Simon, S. M.; Blobel, G.; Zimmerberg, J. 1989. Large aqueous channels in membrane vesicles derived from the rough endoplasmic reticulum of canine pancreas or the plasma membrane of Escherichia coli. *Proc. Natl. Acad. Sci. USA* 86:6176-6180

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

Almost all of the projects examine the transport across membranes of macromolecules from small chemotherapeutics, to proteins, to assembled protein/DNA complexes to the exocytosis of vesicles.

Ongoing:

American Cancer Society Grant # RPG-98-177-01-CDD (Simon) 7/1/98-6/30/06
"Exocytotic organelles, pH and drug resistance in tumor cells"

The major goals of this project have been to quantify the contributions of two mechanisms of drug-resistance in tumor cells i – the plasma membrane based drug-efflux pumps (P-glycoprotein, Pgp and multidrug-resistance associated protein, MRP) ii – the secretion of chemotherapeutics by exocytosis from cytoplasmic organelles. In the past three years this has led to eight publications in peer-reviewed journals. Dr. Simon was the principal investigator on this project.

NIH 1 P20 GM072015 (Simon)- 8/1/2004- 7/31/08
"Imaging single proteins in vivo with quantum dots"

The major goal of this project is to develop the techniques for studying single proteins in living cells with quantum dots. The work focuses completely on the motions of single proteins or the interactions between pairs of proteins and there is no overlap between this proposal and the current application. Dr. Simon is the principal investigator on this project.

NIH/NIBIB 5 R21 EB000979-02 "Large Scale Chemical Screen Against Pathogenic Bacteria" 9/1/02 – 8/31/05
We have used electrophysiological and optical techniques to study how pathogenic bacteria export their toxins. This project uses optical techniques to screen for drugs that selectively target pathogenic bacteria. Dr. Simon is the principal investigator on this proposal.

NSF BES-0322867 "Multicolor total internal reflection fluorescence microscopy" 8/15/03-7/31/06
(previously NSF BES-0110070; 3/1/01 – 2/28/02)
The goal of this project was to develop the technology for doing Total Internal Reflection Microscopy with multiple colors. Dr. Simon was the principle investigator on this project.

Completed in the past three years:

NSF BES-0119468 "In situ optical imaging of multiple proteins". 11/15/01 – 10/31/04
We have been developing a variety of optical techniques to examine cellular function with a particular emphasis on studying the mechanisms of protein sorting and targeting. This project emphasizes the use of protein chemistry to develop new approaches to labeling proteins. Dr. Simon was the principal investigator on this grant.

NIH/NCI R01CA81257 "Non-estrogen receptor tamoxifen activity" 4/1/99 – 3/31/02
The main goals of this project were to characterize the biochemical and cellular basis for the non-estrogen dependent effects of tamoxifen on cells. This has resulted in two publications with two more in preparation. Dr. Simon was the principal investigator on this project.

NIH/NEI 5 R01EY12346-04 "Opsin biogenesis and retinitis pigmentosa" 9/15/02-8/31/04
We have been studying how opsin is targeted to the endoplasmic reticulum (ER) and how it translocates, folds and integrates into the lipid milieu of the ER membrane. Two manuscripts published, two in review. Dr. Simon is the principal investigator on this proposal.